

### **Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

### **Listing of Claims:**

Claims 1-28 Cancelled

29. (New) A composition for treating or preventing arthritis or other degenerative disease, said composition comprising an anti-arthritic or anti-inflammatory polypeptide consisting essentially of at least a portion of the NC4 domain of collagen type IX alpha 1 chain and a carrier.

30 (New) The composition of claim 29, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

31. (New) The composition of claim 29 wherein the polypeptide has an amino acid length of less than 250 amino acids.

32. (New) The composition of claim 29, wherein the NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 70%;
- b) at least 90%; or
- c) 100%.

33. (New) The composition of claim 29, wherein the polypeptide comprises:

- (i) residues Ile21- Gly182 of SEQ ID NO: 1;
- (ii) residues Lys60- Arg181 of SEQ ID NO: 1;
- (iii) residues Arg72- Arg181 of SEQ ID NO: 1;
- (iv) residues Lys98- Gly182 of SEQ ID NO: 1;
- (v) residues Lys123-Gly182 of SEQ ID NO: 1;
- (vi) residues Ile24 - Val208 of SEQ ID NO: 14;
- (vii) residues Asp29 - Val208 of SEQ ID NO: 14,
- (viii) residues Asp29 - Met215 of SEQ ID NO: 14,
- (ix) residues Asp29- Pro209 of SEQ ID NO: 14,

- (x) residues Asp29 - Arg245 of SEQ ID NO: 14,
- (xi) residues Asp29 - Met96 of SEQ ID NO: 14, or
- (xii) residues Trp 108 - Val208 of SEQ ID NO: 14.

34. (New) The composition of claim 29, wherein the polypeptide comprises at least one of SEQ ID NOs: 2-11.

35. (New) A method of inducing tolerance to at least one antigenic component of cartilage in an individual comprising administering to the individual the composition of claim 29.

36. (New) The method of claim 35, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

37. (New) The method of claim 35, wherein the polypeptide has an amino acid length of less than 250 amino acids.

38. (New) The method of claim 35, wherein the NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 70%;
- b) at least 90%, or
- c) 100%.

39. (New) The method of claim 35 wherein the polypeptide comprises:

- (i) residues Ile21- Gly182 of SEQ ID NO: 1;
- (ii) residues Lys60- Arg181 of SEQ ID NO: 1;
- (iii) residues Arg72- Arg181 of SEQ ID NO: 1;
- (iv) residues Lys98- Gly182 of SEQ ID NO: 1;
- (v) residues Lys123-Gly182 of SEQ ID NO: 1;
- (vi) residues Ile24 - Val208 of SEQ ID NO: 14;
- (vii) residues Asp29 - Val208 of SEQ ID NO: 14,
- (viii) residues Asp29 - Met215 of SEQ ID NO: 14,
- (ix) residues Asp29- Pro209 of SEQ ID NO: 14,
- (x) residues Asp29 - Arg245 of SEQ ID NO: 14,
- (xi) residues Asp29 - Met96 of SEQ ID NO: 14, or

(xii) residues Trp108 - Val208 of SEQ ID NO: 14.

40. (New) The method of claim 35, wherein the polypeptide comprises at least one of SEQ ID NOs: 2-11.

41. (New) The method of claim 35, wherein the individual is a naive individual.

42. (New) A method for treating or preventing a degenerative condition or disease in an individual comprising administering to the individual the composition of claim 29.

43. (New) The method of claim 42, wherein the degenerative condition or disease is arthritis or a musculoskeletal degenerative condition.

44. (New) The method of claim 43, wherein the degenerative condition or disease is rheumatoid arthritis, osteoarthritis, disc degeneration, or osteoporosis.

45. (New) The method of claim 42, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

46. (New) The method of claim 42, wherein the polypeptide has an amino acid length of less than 250 amino acids.

47. (New) The method of claim 42, wherein the NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 70%
- b) at least 90%, or
- c) 100%.

48. (New) The method of claim 42 wherein the polypeptide comprises:

- (i) residues Ile21- Gly182 of SEQ ID NO: 1;
- (ii) residues Lys60- Arg181 of SEQ ID NO: 1;
- (iii) residues Arg72- Arg181 of SEQ ID NO: 1;
- (iv) residues Lys98- Gly182 of SEQ ID NO: 1;

- (v) residues Lys123-Gly182 of SEQ ID NO: 1;
- (vi) residues Ile24 - Val208 of SEQ ID NO: 14;
- (vii) residues Asp29 - Val208 of SEQ ID NO: 14,
- (viii) residues Asp29 - Met215 of SEQ ID NO: 14,
- (ix) residues Asp29- Pro209 of SEQ ID NO: 14,
- (x) residues Asp29 - Arg245 of SEQ ID NO: 14,
- (xi) residues Asp29 - Met96 of SEQ ID NO: 14, or
- (xii) residues Trp108 - Val208 of SEQ ID NO: 14.

49. (New) The method of claim 42, wherein the polypeptide comprises at least one of SEQ ID NOs: 2-11.

50. (New) The method of claim 42, wherein the individual is a naive individual.

51. (New) A method for isolating a polypeptide having anti-arthritic or anti-inflammatory activity comprising:

- (i) incubating a connective tissue in a buffered autolysis medium to release a mixture of polypeptides containing GAG polypeptides and non-GAG polypeptides;
- (ii) fractionating the polypeptides by size to produce a fraction of proteins having a molecular weight of less than 30 KDa;
- (iii) separating GAG-polypeptides from non-GAG polypeptides; and
- (iv) recovering non-GAG polypeptides having a molecular weight less than 30 KDa, and having anti-arthritic or anti-inflammatory activity.

52. (New) The method of claim 51, wherein the autolysis medium has a pH range of:

- a) about pH 2.5 to about pH 8.5;
- b) pH 3.5 to about pH 8;
- c) pH 4 to about pH 7; or
- d) pH 4.5 to about pH 7.

53. (New) A method for preventing an autoimmune response in an individual to at least one antigenic component of cartilage comprising administering the individual the composition of

claim 29.

54. (New) The method of claim 53, wherein the polypeptide has a molecular weight of:

- a) less than 30,000Da, or
- b) less than 30,000Da and greater than or equal to 10,000 Da.

55. (New) The method of claim 53, wherein the polypeptide has an amino acid length of less than 250 amino acids.

56. (New) The method of claim 53, wherein the NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 70%
- b) at least 90%, or
- c) 100%.

57. (New) The method of claim 53, wherein the polypeptide comprises:

- (i) residues Ile21- Gly182 of SEQ ID NO: 1;
- (ii) residues Lys60- Arg181 of SEQ ID NO: 1;
- (iii) residues Arg72- Arg181 of SEQ ID NO: 1;
- (iv) residues Lys98- Gly182 of SEQ ID NO: 1;
- (v) residues Lys123-Gly182 of SEQ ID NO: 1;
- (vi) residues Ile24 - Val208 of SEQ ID NO: 14;
- (vii) residues Asp29 - Val208 of SEQ ID NO: 14,
- (viii) residues Asp29 - Met215 of SEQ ID NO: 14,
- (ix) residues Asp29- Pro209 of SEQ ID NO: 14,
- (x) residues Asp29 - Arg245 of SEQ ID NO: 14,
- (xi) residues Asp29 - Met96 of SEQ ID NO: 14, or
- (xii) residues Trp108 - Val208 of SEQ ID NO: 14.

58. (New) The method of claim 53, wherein the polypeptide comprises at least one of SEQ ID NOs: 2-11.

59. (New) A method of inducing cartilage formation in an individual, comprising administering to the individual the polypeptide produced by the method of claim 29.

60. (New) The method of claim 59, wherein the polypeptide has a molecular weight of:
- less than 30,000Da, or
  - less than 30,000Da and greater than or equal to 10,000 Da.
61. (New) The method of claim 59, wherein the polypeptide has an amino acid length of less than 250 amino acids.
62. (New) The method of claim 59, wherein the NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:
- at least 70%
  - at least 90%, or
  - 100%.
63. (New) The method of claim 59, wherein the polypeptide comprises:
- residues Ile21- Gly182 of SEQ ID NO: 1;
  - residues Lys60- Arg181 of SEQ ID NO: 1;
  - residues Arg72- Arg181 of SEQ ID NO: 1;
  - residues Lys98- Gly182 of SEQ ID NO: 1;
  - residues Lys123-Gly182 of SEQ ID NO: 1;
  - residues Ile24 - Val208 of SEQ ID NO: 14;
  - residues Asp29 - Val208 of SEQ ID NO: 14,
  - residues Asp29 - Met215 of SEQ ID NO: 14,
  - residues Asp29- Pro209 of SEQ ID NO: 14,
  - residues Asp29 - Arg245 of SEQ ID NO: 14,
  - residues Asp29 - Met96 of SEQ ID NO: 14, or
  - residues Trp108 - Val208 of SEQ ID NO: 14.
64. (New) The method of claim 59, wherein the polypeptide of collagen type IX alpha 1 chain comprises at least one of SEQ ID NOs: 2-11.